INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 24, no. 2, 277-284 (2011)

EDITORIAL

PATHOGENESIS AND CLINICAL APPROACHES TO ANTICONVULSANT HYPERSENSITIVITY SYNDROME: CURRENT STATE OF KNOWLEDGE

A. SCAPARROTTA[1], A. VERROTTI[1], N.P. CONSILVIO[1], A. CINGOLANI[1], S. DI PILLO[1], M. DI GIOACCHINO[2], M. VERINI[1] and F. CHIARELLI[1]

[1]Department of Paediatrics, "G. d'Annunzio" University, Chieti; [2]Allergy Related Disease Unit, "G. d'Annunzio" University, Chieti, Italy

Received February 3, 2011 – Accepted April 13, 2011

Anticonvulsant hypersensitivity syndrome (AHS) is a rare, but severe and potentially fatal, adverse reaction that occurs in patients who are treated with commonly used older anticonvulsant drugs (phenytoin, carbamazepine and phenobarbital) and/or with some newer agents (lamotrigine). Paediatric patients are at an increased risk for the development of AHS for the higher incidence of seizure disorder in the first decade of life. Hypersensitivity reactions range from simple maculopapular skin eruptions to a severe life-threatening disorder. AHS is typically associated with the development of skin rash, fever and internal organ dysfunctions. Recent evidence suggests that AHS is the result of a chemotoxic and immunologically-mediated injury, characterized by skin and mucosal bioactivation of antiepileptic drugs and by major histocompatibility complex-dependent clonal expansion of T cells. Early recognition of AHS and withdrawal of anticonvulsant therapy are essential for a successful outcome. *In vivo* and *vitro* tests can be helpful for the diagnosis that actually depends essentially on clinical recognition.

0394-6320 (2011)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 24, no. 2, 285-296 (2011)

EDITORIAL

MOLECULAR APPROACH BY PCR IS THE BEST METHOD TO DETECT THE PRESENCE OF *CHLAMYDIA TRACHOMATIS* AND TO DEFINE THE TRUE AGENT OF OCULAR BACTERIAL INFLAMMATION

P.E. GALLENGA[1], M. DEL BOCCIO[1], M. RAPINESE[1], A. DI IORIO[2], E. TONIATO[3] and S. MARTINOTTI[3]

[1]Dept. Surgical Science Clinical Experimental, Section of Ophthalmology; [2]Dept. of Medicine and Aging Sciences; [3]Dept. of Oncology and Neuroscience Biomedical Sciences. Faculty of Medicine, "G. d'Annunzio" University Chieti-Pescara

Received January 31, 2011 – Accepted April 18, 2011

***Chlamydia trachomatis* (Ct) is an atypical agent for acute, subclinical and chronic conjunctivitis in developed countries, as stated by the International League against Trachoma. In order to evaluate the presence of Ct, from a total of 3,520 patients visiting the consulting room of the Eye Clinic of G. d'Annunzio University of Chieti, Italy from 2006-2008, we enrolled 171 patients affected by occasional mild, moderate or severe conjunctivitis in a three-arm prospective open study, using traditional analysis such as Immune Fluorescent Assay and Enzyme–Linked Fluorescent Assay (IFA and ELFA) and molecular analysis with Polymerase Chain Reaction (PCR) procedure for Ct DNA research (Ct DNA). At the same time, microbiological culture was carried out for common germs and mycetes. These patients were analyzed at different subsequent times. In the first arm (Group A) of 82 patients with IFA and ELFA only 10 people (12.2%) resulted positive to Ct infection with both methods. The presence of Ct was never alone, but always overlapped with contaminants, like corynebacteria, staphylococci, streptococci and colonbacteria, randomly distributed, while no growth of mycetes was observed. Of these positive patients, only one 47-year-old female, suffering from a moderate form of ocular chlamydial infection, showed serological conversion against this infection; furthermore, this female had also been suffering from reactive arthritis for sometime. In the second arm (Group B) of 89 patients, we carried out PCR for Ct detection: 82 (94.25%) were found positive to Ct – DNA research, with common germ growth randomly associated, without sex or age prevalence, as in group A; no mycetes were found. The third arm (Group C) included 37 negative patients from Group A with severe or moderate chronic conjunctivitis, randomly recruited between relapsing cases, with the addition of the single previously positive seroconversion case, for a total of 38 patients, who were re-evaluated by PCR Ct-DNA analysis. All these patients, negative to IFA and ELFA, were positive to Ct-DNA analysis. These data indicate a higher rate of Ct infection in patients with severe or moderate chronic conjunctivitis, resistant to usual therapies even after eradication of common germs, thus showing the advantage of introducing this molecular technique of analysis in mild to severe chronic or recurrent conjunctivitis.**

0394-6320 (2011)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 24, no. 2, 297-304 (2011)

EDITORIAL

NOVEL STRATEGIES FOR THE DEVELOPMENT OF A VACCINE FOR *PARIETARIA* ALLERGY

A. BONURA and P. COLOMBO

Istituto di Biomedicina ed Immunologia Molecolare "Alberto Monroy", Consiglio Nazionale delle Ricerche, Palermo, Italy

Received January 20, 2011 – Accepted April 29, 2011

Specific immunotherapy is a well established and clinically proved strategy to cure allergic reactions. The impressive boost of knowledge derived from DNA recombinant technology applied to this field allowed the identification, cloning and expression of several clinically relevant allergens. Recombinant allergens can be easily produced in a pure and reproducible way with immunological properties comparable to natural allergens and matching the requirements of pharmaceutical companies. *Parietaria* pollinosis is a major health problem in the Mediterranean basin with prolonged symptoms. In this review we will discuss the rational approaches to design hypoallergenic derivatives of the major allergens of this pollen, their immunological properties and possible clinical future implications.

0394-6320 (2011)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 24, no. 2, 305-311 (2011)

EDITORIAL

ALLERGIC INFLAMMATION: ROLE OF CYTOKINES WITH SPECIAL EMPHASIS ON IL-4

A. SAGGINI[1], G. MACCAURO[2], D. TRIPODI[3], M.A. DE LUTIIS[4], F. CONTI[5], P. FELACO[4], M. FULCHERI[6], R. GALZIO[7], A. CARAFFA[8], P. ANTINOLFI[8], M. FELACO[5], F. PANDOLFI[9], G. SABATINO[10], G. NERI[11] and Y.B. SHAIK-DASTHAGIRISAHEB[12]

[1]Department of Dermatology, University of Rome Tor Vergata, Rome, Italy; [2]Department of Orthopaedics, Catholic University of Rome, Rome, Italy; [3]School of Dentistry, University of Chieti, Italy; [4]Department of Human Dynamics, University of Chieti, Italy; [5]Gynecology Division, Vasto Hospital, Vasto, Italy; [6]Department of Clinical Psychology, University of Chieti, Italy; [7]Department of Health Sciences, University of L'Aquila, Italy; [8]Orthopaedics Division, University of Perugia, Perugia, Italy; [9]Institute of Internal Medicine, Catholic University, Rome, Italy; [10]Neonatology Division, University of Chieti, Italy; [11]Department of ORL, University of Chieti, Chieti, Italy; [12]Department of Medicine, Boston University School of Medicine, Boston, MA, USA

Received February 16, 2011 – Accepted 2 May, 2011

This review examines recent articles on the relationship of cytokines to allergy and inflammation with particular emphasis on interleukin (IL)-4. The objective of this article is therefore to review published studies to identify cytokines consistently involved in allergic inflammation. Proinflammatory cytokines, including IL-4, IL-5, IL-13 and GM-CSF along with TNF-alpha play a role in allergen-induced airway leukocyte recruitment and these cytokines can be generated by T mast cells and other cells. In addition, IL-9, IL-25, IL-33, IL-17, IL-27 and IFN-γ are deeply involved in the regulation of asthma. Blocking the effect of these proinflammatory cytokines might provide new therapeutic approaches for the control of allergy and inflammation.

0394-6320 (2011)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 24, no. 2, 313-322 (2011)

EDITORIAL

PARAQUAT- AND ROTENONE-INDUCED MODELS OF PARKINSON'S DISEASE

R. NISTICÒ[1,2], B. MEHDAWY[3], S. PICCIRILLI[4] and N. MERCURI[2,5]

[1]Department of Pharmacobiology, University of Calabria, Rende; [2]IRCCS Santa Lucia Foundation, Rome; [3]IRCCS National Neurological Institute C. Mondino Foundation, Pavia; [4]Pharmaceutical Biotechnology Center, University of Rome "Tor Vergata", Rome; [5]Neurological Clinic, University of Rome "Tor Vergata", Rome, Italy

Received February 2, 2011 – Accepted May 4, 2011

Parkinson's disease (PD) is a neurodegenerative disorder mainly characterized by a loss of dopaminergic (DA) neurons in the substantia nigra *pars compacta*. In recent years, several new genes and environmental factors have been implicated in PD, and their impact on DA neuronal cell death is slowly emerging. However, PD etiology remains unknown, whereas its pathogenesis begins to be clarified as a multifactorial cascade of deleterious factors. Recent epidemiological studies have linked exposure to environmental agents, including pesticides, with an increased risk of developing the disease. As a result, over the last two decades the 'environmental hypothesis' of PD has gained considerable interest. This speculates that agricultural chemicals in the environment, by producing selective dopaminergic cell death, can contribute to the development of the disease. However, a causal role for pesticides in the etiology of PD has yet to be definitively established. Importantly, most insights into PD pathogenesis came from investigations performed in experimental models of PD, especially those produced by neurotoxins. This review presents data obtained in our laboratories along with current views on the neurotoxic actions induced by the two most popular parkinsonian pesticide neurotoxins, namely paraquat and rotenone. Although confined to these two chemicals, mechanistic studies underlying dopaminergic cell death are of the utmost importance to identify new drug targets for the treatment of PD.

0394-6320 (2011)

ANTI-TNF-α ANTIBODY (INFLIXIMAB) THERAPY SUPPORTS THE RECOVERY OF eNOS AND VEGFR2 PROTEIN EXPRESSION IN ENDOTHELIAL CELLS

I. ALTORJAY[1], Z. VERÉB[2], Z. SERFŐZŐ[3], I. BACSKAI[2], R. BÁTORI[4], F. ERDŐDI[4], M. UDVARDY[1], S. SIPKA[5], Á. LÁNYI[2], É. RAJNAVÖLGYI[2] and K. PALATKA[1]

[1]2nd Department of Medicine, Medical and Health Science Center, University of Debrecen, Debrecen; [2]Institute of Immunology, Medical and Health Science Center, University of Debrecen, Debrecen; [3]Department of Experimental Zoology, Balaton Limnological Research Institute, Hungarian Academy of Sciences, Tihany; [4]Department of Medical Chemistry, Medical and Health Science Center, University of Debrecen, Debrecen; [5]3rd Department of Internal Medicine, Medical and Health Science Center, University of Debrecen, Debrecen, Hungary

Received January 20, 2011 – Accepted May 6, 2011

The first three authors authors contributed equally to the experiments and the manuscript

The aim of this study is to investigate the effect of sera obtained from patients of Crohn's disease treated by anti-TNF-α antibody (infliximab) on the expression of endothelial nitric oxide synthase (eNOS) and vascular endothelial growth factor receptor-2 (VEGFR2) protein in human umbilical vein endothelial cells (HUVEC) cultured *in vitro*. HUVEC was cultured in the presence of sera derived from patients before and after treatment, or from healthy individuals. Effects of sera on the expression of eNOS and VEGFR2 were monitored by determination of mRNA and protein levels using real time quantitative PCR and Western blot analysis, respectively. The serum of Crohn's patients contained elevated levels of TNF-α (34±1.80 pg/mL), which resulted in a decrease in the protein level of eNOS in HUVEC with a simultaneous induction of VEGFR2. Infliximab treatment normalized the expression level of these proteins by decreasing TNF-α level, particularly in those cases when clinical healing was also recorded, and it also conferred restitution of the level of angiogenic cytokines. Results suggest that altered angiogenesis possibly contributes to the initiation and perpetuation of inflammatory processes in Inflammatory Bowel Disease (IBD). Endothelial dysfunction, a selective feature of Crohn's disease is beneficially affected by intravascular TNF-α neutralization.

0394-6320 (2011)

THE EFFECTS OF CAPTOPRIL ON CARDIAC REGRESSION, BLOOD PRESSURE AND BRADYKININ COMPONENTS IN DIABETIC WISTAR KYOTO RATS

J.N. SHARMA[1] and U. KESAVARAO[2]

[1]Department of Applied Therapeutics, Faculty of Pharmacy, Health Sciences Centre Kuwait University, Safat, Kuwait; [2]University Science Malaysia, Malaysia

Received January 25, 2011 – Accepted April 6, 2011

The present study examined the left ventricular wall thickness (LVWT), total urinary kallikrein, total plasma kininogen and mean arterial blood pressure (MABP) in diabetic and non-diabetic Wistar Kyoto (WKY) rats. The MABP was significantly raised (P<0.01) in diabetic WKY rats compared to the respective controls. The LVWT was also significantly (P<0.01) increased in diabetic WKY rats than that of control WKY rats. The mean total urinary kallikrein level and the mean total plasma kininogen level were higher (P<0.01) in diabetic WKY rats, when these rats were treated with captopril (40 mg/kg and 80 mg/kg) against the mean value obtained from control WKY rats. In conclusion, this investigation suggests that diabetes induced in these rats can cause hypertension, increased LVWT and changes in the BK-forming components. Captopril treatment caused reduction in MABP, regression of LVWT and alterations in bradykinin (BK)-forming components. The possible significance of these observations is discussed.

0394-6320 (2011)

EUGENOLOL AND GLYCERYL-ISOEUGENOL SUPPRESS LPS-INDUCED INOS EXPRESSION BY DOWN-REGULATING NF-κB AND AP-1 THROUGH INHIBITION OF MAPKS AND AKT/IκBα SIGNALING PATHWAYS IN MACROPHAGES

J.L. YEH[1], J.H. HSU[2,3], Y.S. HONG[1], J.R. WU[2,3], J.C. LIANG[4], B.N. WU[1], I.J. CHEN[1] and S.F. LIOU[5]

[1]Department and Graduate Institute of Pharmacology, College of Medicine, Kaohsiung Medical University, Kaohsiung; [2]Department of Paediatrics, Kaohsiung Medical University Hospital, Kaohsiung; [3]Department of Paediatrics, Faculty of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung; [4]Graduate Institute of Engineering, National Taiwan University of Science and Technology, Taipei; [5]Department of Pharmacy, Chia-Nan University of Pharmacy and Science, Tainan, Taiwan

Received October 25, 2010 – Accepted April 14, 2011

Eugenol and isoeugenol, two components of clover oil, have been reported to possess several biomedical properties, such as anti-inflammatory, antimicrobial and antioxidant effects. This study aims to examine the anti-inflammatory effects of eugenol, isoeugenol and four of their derivatives on expression of inducible nitric oxide synthase (iNOS) activated by lipopolysaccharide (LPS) in mouse macrophages (RAW 264.7), and to investigate molecular mechanisms underlying these effects. We found that two derivatives, eugenolol and glyceryl-isoeugenol, had potent inhibitory effects on LPS-induced upregulation of nitrite levels, iNOS protein and iNOS mRNA. In addition, they both suppressed the release of tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β) induced by LPS. Moreover, they both attenuated the DNA binding of NF-κB and AP-1, phosphorylation of inhibitory κBα (IκBα), and nuclear translocation of p65 protein induced by LPS. Finally, we demonstrated that glyceryl-isoeugenol suppressed the phosphorylation of ERK1/2, JNK and p38 MAPK, whereas eugenolol suppressed the phosphorylation of ERK1/2 and p38 MAPK. Taken together, these results suggest that that eugenolol and glyceryl-isoeugenol suppress LPS-induced iNOS expression by down-regulating NF-κB and AP-1 through inhibition of MAPKs and Akt/IκBα signaling pathways. Thus, this study implies that eugenolol and glyceryl-isoeugenol may provide therapeutic benefits for inflammatory diseases.

0394-6320 (2011)

COMPLEMENT SYSTEM AND RHEUMATOID ARTHRITIS: RELATIONSHIPS WITH AUTOANTIBODIES, SEROLOGICAL, CLINICAL FEATURES, AND ANTI-TNF TREATMENT

G. DI MUZIO[1], C. PERRICONE[2], E. BALLANTI[1], B. KROEGLER[1], E. GRECO[1], L. NOVELLI[1], P. CONIGLIARO[1], P. CIPRIANI[3], R. GIACOMELLI[3] and R. PERRICONE[1]

[1]Rheumatology, Allergology and Clinical Immunology, Department of Internal Medicine, University of Rome Tor Vergata, Rome; [2]Reumatology, Department of Internal Medicine and Medical Specialities, Sapienza University of Rome, Rome; [3]Rheumatology, University of L'Aquila, L'Aquila, Italy

Received February 14, 2011 – Accepted may 3, 2011

The first two authors contributed equally to this work

Autoantibodies (rheumatoid factor, RF; anti-citrullinated-protein antibodies, ACPA) and complement system are involved in rheumatoid arthritis (RA). ACPA and anti-TNF agents are capable of in vitro modulating complement activity. We investigated the relationships between complement, autoantibodies, and anti-TNF treatment *in vivo*. One-hundred fourteen RA patients (89F/25M), diagnosed according to 1987 ACR criteria, and 30 healthy controls were enrolled. Serological analysis included ESR, CRP, complement C3, C4 and CH50, RF and ACPA (ELISA, cut-off>20U/ml). Split-products (SP) of C3 and B were studied by immunoelectrophoresis/counterimmunoelectrophoresis. Seventy-six patients started anti-TNF treatment and were studied at baseline and after 22 weeks. Disease activity was measured with DAS28 and response to therapy with EULAR criteria. At baseline, RA patients showed significantly higher levels of C3 and C4 than controls (C3 127.9±26.5 vs 110±25mg/dl, P=0.0012; C4 29.7±10.2 vs 22.7±8.3mg/dl, P=0.0003). No differences in C3, C4 and CH50 levels were observed between ACPA+ (n=76) and ACPA- (n=38) patients. After 22 weeks of anti-TNF, C3, C4 and RF were significantly reduced (P<0.003, <0.005 and <0.04, respectively) and RF changes showed negative correlation with CH50. SP of C3 and B were observed neither at baseline nor after 22 weeks. DAS28 significantly improved after 22 weeks. Patients showing higher baseline C3 or lower reduction of C3 levels after 22 weeks had a worse EULAR outcome (χ^2=22.793, P<0.001). RF levels seem to correlate with complement CH50. The presence of high levels of C3 in RA patients may reflect a pro-inflammatory status and represent a negative prognostic factor for anti-TNF therapy.

0394-6320 (2011)

A PILOT STUDY EVALUATING THE CLINICAL AND IMMUNOMODULATORY EFFECTS OF AN ORALLY ADMINISTERED EXTRACT OF *DENDROBIUM HUOSHANENSE* IN CHILDREN WITH MODERATE TO SEVERE RECALCITRANT ATOPIC DERMATITIS

K-G. WU[1], T-H. LI[1, 2], C-J. CHEN[1], H-I. CHENG[1] and T-Y. WANG[1]

[1]Department of Pediatrics, Taipei Veterans General Hospital and National Yang-Ming University, Taipei; [2]Department of Pediatrics, Hualien Armed Forces General Hospital, Hualien, Taiwan

Received September 19, 2010 – Accepted January 8, 2011

Atopic dermatitis (AD) is a common inflammatory skin disorder for which few safe and effective systemic treatments are available. To test the clinical and immunomodulatory effects of a crude polysaccharide fraction isolated from *Dendrobium huoshanense* for the treatment of AD, we conducted a pilot, uncontrolled case series study. Twenty-seven patients aged 4-18 years (mean±SD, 10.82±4.4) with AD that had not responded to topical therapy were treated with polysaccharide derived from *D. huoshanense* for 4 weeks and followed-up for another 4 weeks. Progression of AD was determined with the Lund-Browder chart for children, the Investigator's Global Atopic Dermatitis Assessment (IGADA), and the Scoring Atopic Dermatitis (SCORAD) at weeks 0, 2, 4, and 8. Serum levels of cytokines were evaluated. Safety was determined with laboratory and clinical tests. The lesion area, IGADA score, total SCORAD result, and score for sleeplessness decreased significantly from weeks 0 to 4, but did not change significantly between weeks 4 and 8. The scores for subjective symptoms and pruritus decreased significantly from week 0 to week 4 and increased significantly from week 4 to week 8. Serum levels of IL-5, IL-13, IFN-γ, and TGF-β1 decreased significantly between weeks 0 and 4 and between weeks 0 and 8. No significant difference in the levels of IL-10 was found. The polysaccharide from *D. huoshanense* reduced the levels of some cytokines associated with AD and had beneficial effects on symptoms. No serious adverse effects occurred when it was administered orally for 4 weeks.

0394-6320 (2011)

EVALUATION OF THYROID GLAND FUNCTION IN CHILDREN WITH OBSTRUCTIVE APNEA HYPOPNEA SYNDROME

A.V. SAKELLAROPOULOU[1], M.N. HATZISTILIANOU[1], M.N. EMPORIADOU[1], V.TH. AIVAZIS[2], I. ROUSSO[1] and F. ATHANASIADOU-PIPEROPOULOU[1]

[1]2nd Paediatric Department of Aristotle University of Thessaloniki, AHEPA Hospital, Thessaloniki; [2]1st Paediatric Department, Hippokration General Hospital, Thessaloniki, Greece

Received January 28, 2011 – Accepted May 3, 2011

Patients with obstructive sleep apnea hypopnea syndrome (OSAHS) and thyroid function abnormalities, such as hypothyroidism and Hashimoto's thyroiditis, usually have closely resembling clinical features. Differentiation between these disorders is made more difficult because hypothyroid patients are also at risk for secondary sleep-disordered breathing. The aim of our study is to evaluate the prevalence of thyroid function abnormalities in children with OSAHS. Forty-four children (15 females: 29 males), 2.5-14.5 (7.43±2.98) years old were studied with overnight polysomnography. Biochemical screening of thyroid gland function was also carried out. Patients were judged to have OSAHS based mainly on the evaluation of Apnea Hypopnea index per hour of sleep (AHI). 15/44 (34.1%) children had mild OSAHS, 17/44 (38.6%) moderate and 12/44 (27.3%) severe OSAHS. Hypothyroidism was recorded only in 5/44 (11.4%) and Hashimoto's thyroiditis in 3/44 (6.8%) of OSAHS patients. Two patients with hypothyroidism showed mild and three severe OSAHS, while from the 3 children with Hashimoto's thyroiditis one presented mild, one moderate and one severe degree of OSAHS. Although the majority of studies in bibliography worldwide do not consider necessary the systemic evaluation of thyroid gland function in patients with breathing disorders during sleep, it seems that in children this type of screening is required for the differential diagnosis between primary sleep apnea and hypothyroid sleep-disordered breathing in order to differentiate these two conditions. Therefore, the laboratory investigation of thyroid gland function could be considered necessary.

0394-6320 (2011)

CHARACTERISTICS OF PATIENTS WITH RESPIRATORY ALLERGY IN FRANCE AND FACTORS INFLUENCING IMMUNOTHERAPY PRESCRIPTION: A PROSPECTIVE OBSERVATIONAL STUDY (REALIS)

M. MIGUERES[1], J.-F. FONTAINE[2], T. HADDAD[3], M. GROSCLAUDE[4], F. SAINT-MARTIN[5], D. BEM DAVID[6] and B. CRESTANI[7]

[1]Clinique de l'Union, Saint-Jean, Toulouse; [2]Cabinet d'Allergologie, Reims; [3]Cabinet d'Allergologie, Paris; [4]Cabinet d'Allergologie, Centre Claude-Bernard, Guilherand, Granges; [5]Cabinet d'Allergologie, Villebon sur Yvette; [6]Stallergenes SA, Antony; [7]Service de Pneumologie A, Hôpital Bichat, Paris, France

Received February 4, 2011 – Accepted May 5, 2011

To describe the sensitization profile of respiratory allergies in France, identifying factors influencing the prescription of allergen immunotherapy (AIT) [Transversal phase (T)], and assess treatment efficacy, tolerability, compliance and satisfaction [Longitudinal phase (L)]. French allergists (600) and pneumo-allergists (600) were offered participation and asked to recruit the first 20 new patients with allergic rhinitis (AR) and/or asthma, consulting for a first time allergy check-up with skin prick-test (T), and 5 patients sensitized to pollens (skin test and/or specific IgE) for whom SLIT with pollens was prescribed (L). In the T phase, 2,714 patients were recruited by 169 specialists, mostly allergists (76.5%). The majority (98%) suffered from AR, alone (57.7%) or with asthma (40.3%) and 80.3% suffered from moderate-to-severe rhinitis, mostly persistent (65.8%). Asthma, when present, was mostly intermittent (63.7%) or mild persistent (20.1%). Sensitization to house dust mites was the most common (64.5%), followed by grass pollens (61.5%), tree pollens (41.6%) and cat danders (30.5%). Poly-sensitization was seen in 73.6% of patients. AIT, mostly sublingual, was recommended in 55.6% of the patients, mostly (78.1%) because of insufficient control with symptomatic treatments. The overall impact of symptoms on QOL, positive skin test to grass pollens, ocular pruritus and/or nasal obstruction and moderate-to-severe rhinitis were significant predictors of SLIT prescription. Poly-sensitization or concomitant asthma were not seen as deterrents. Most patients consulting a specialist for allergy testing suffer from moderate-to-severe rhinitis. Treatment in current practice includes immunotherapy in half of the patients, and follows ARIA recommendations.

0394-6320 (2011)

INTRANASAL FLUNISOLIDE TREATMENT IN PATIENTS WITH NON-ALLERGIC RHINITIS

A. VARRICCHIO[1], M. CAPASSO[1], A. DE LUCIA[1], F. AVVISATI[1], A.M. VARRICCHIO[2], G. BETTONCELLI[3] and G. CIPRANDI[4]

[1]U.O.C. O.R.L. - Ospedale San Gennaro, ASL Na1, Naples; [2]U.O.C. di O.R.L. - Azienda Ospedaliera Pediatrica Santobono Pausilipon, Naples; [3]SIMG - Società Italiana di Medicina Generale, Firenze; [4]Dipartimento di Medicina Interna, Azienda Ospedaliera Universitaria San Martino, Genoa, Italy

Received October 19, 2010 - Accepted March 1, 2011

Non-allergic rhinitis (NAR) is a heterogeneous disease, characterized by nasal hyperreactivity and inflammation. Its treatment is still debated, intranasal corticosteroids may be an option. The present study is aimed at evaluating the effect of the use of intranasal flunisolide in patients with NAR, considering both clinical and cytological parameters. Sixty patients were treated with intranasal flunisolide (30) or saline solution (30) for 8 weeks. Symptom severity, turbinate size, and inflammatory cell counts were assessed, before and after treatment. Intranasal flunisolide induced a significant reduction of symptoms, turbinate size, and cellular infiltrate. Thus, intranasal flunisolide might be a therapeutic option for NAR.

0394-6320 (2011)

BIOLOGICAL EFFECTS OF LOW FREQUENCY HIGH INTENSITY ULTRASOUND APPLICATION ON *EX VIVO* HUMAN ADIPOSE TISSUE

P. PALUMBO[1], B. CINQUE[1], G. MICONI[1], C. LA TORRE[1], G. ZOCCALI[1], N. VRENTZOS[1], A.R. VITALE[1], P. LEOCATA[1], D. LOMBARDI[1], C. LORENZO[1], B. D'ANGELO[2], G. MACCHIARELLI[1], A. CIMINI[2], M.G. CIFONE[1] and M. GIULIANI[1]

[1]Department of Health Sciences and [2]Department of Basic and Applied Biology, University of L'Aquila, L'Aquila, Italy

Received October 11, 2010 – Accepted March 8, 2011

The first two authors contributed equally to this work

In the present work the effects of a new low frequency, high intensity ultrasound technology on human adipose tissue *ex vivo* were studied. In particular, we investigated the effects of both external and surgical ultrasound-irradiation (10 min) by evaluating, other than sample weight loss and fat release, also histological architecture alteration as well apoptosis induction. The influence of saline buffer tissue-infiltration on the effects of ultrasound irradiation was also examined. The results suggest that, in our experimental conditions, both transcutaneous and surgical ultrasound exposure caused a significant weight loss and fat release. This effect was more relevant when the ultrasound intensity was set at 100% (~ 2.5 W/cm², for external device; ~19-21 W/cm², for surgical device) compared to 70% (~ 1.8 W/cm² for external device; ~13-14 W/cm² for surgical device). Of note, the effectiveness of ultrasound was much higher when the tissue samples were previously infiltrated with saline buffer, in accordance with the knowledge that ultrasonic waves in aqueous solution better propagate with a consequently more efficient cavitation process. Moreover, the overall effects of ultrasound irradiation did not appear immediately after treatment but persisted over time, being significantly more relevant at 18 h from the end of ultrasound irradiation. Evaluation of histological characteristics of ultrasound-irradiated samples showed a clear alteration of adipose tissue architecture as well a prominent destruction of collagen fibers which were dependent on ultrasound intensity and most relevant in saline buffer-infiltrated samples. The structural changes of collagen bundles present between the lobules of fat cells were confirmed through scanning electron microscopy (SEM) which clearly demonstrated how ultrasound exposure induced a drastic reduction in the compactness of the adipose connective tissue and an irregular arrangement of the fibers with a consequent alteration in the spatial architecture. The analysis of the composition of lipids in the fat released from adipose tissue after ultrasound treatment with surgical device showed, in agreement with the level of adipocyte damage, a significant increase mainly of triglycerides and cholesterol. Finally, ultrasound exposure had been shown to induce apoptosis as shown by the appearance DNA fragmentation. Accordingly, ultrasound treatment led to down-modulation of procaspase-9 expression and an increased level of caspase-3 active form.

0394-6320 (2011)

ANALYSIS OF INFLAMMATORY AND IMMUNE RESPONSE BIOMARKERS IN SPUTUM AND EXHALED BREATH CONDENSATE BY A MULTI-PARAMETRIC BIOCHIP ARRAY IN CYSTIC FIBROSIS

C. COLOMBO[1], N. FAELLI[1], A.S. TIRELLI[2], F. FORTUNATO[3], A. BIFFI[1], L. CLAUT[1], L. CARIANI[1], V. DACCÒ[1], R. PRATO[3] and M. CONESE[4]

[1]Cystic Fibrosis Centre and [2]Laboratory of Clinical Pathology, Fondazione IRCSS Ca' Granda Ospedale Maggiore Policlinico, Milan; [3]Department of Medical Sciences and [4]Department of Biomedical Sciences, University of Foggia Italy

Received October 6, 2010 – Accepted March 25, 2011

Cystic Fibrosis (CF) lung disease is characterized by high levels of cytokines and chemokines in the airways, producing chronic inflammation. Non-invasive biomarkers, which are also specific for the inflammatory and immune responses, are urgently needed to identify exacerbations and evaluate therapeutic efficacy. The aim of this study is to evaluate the association of sputum and exhaled breath condensate (EBC) biomarker changes with clinical exacerbation and response to therapy. We studied the simultaneous presence and concentration of twelve cytokines and growth factors (EGF, IL-1α, IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, IFN-γ, MCP-1, TNF-α and VEGF) by a multi-parametric biochip array in sputum and EBC of 24 CF patients before, after 6 and 15 days of therapy, and 15 days after the end of treatment for an acute exacerbation. Correlations with functional respiratory tests (FEV_1, FVC) and the systemic marker C-reactive protein (CRP) were looked for. In sputum, before therapy, VEGF and IL-1β levels positively correlated with the respiratory function and CRP. Sputum IL-1α, IL-1β IL-4, IL-10, TNF-α, and VEGF significantly decreased, while EGF increased, during therapy. IL-8 and IL-4 levels negatively correlated with the respiratory function at 15 and 30 days from the start of therapy, respectively. IL-4, IL-6, IL-10 and TNF-α positively correlated with CRP during therapy. Although some EBC biomarkers correlated with respiratory function and CRP, no significant associations with these clinical parameters were found. Sputum IL-1β and VEGF might be considered biomarkers of an acute exacerbation in CF patients. A panel of sputum cytokines and growth factors may better describe the response to intravenous antibiotic treatment of CF than one single systemic marker.

0394-6320 (2011)

PROCALCITONIN, C-REACTIVE PROTEIN, INTERLEUKIN-6, AND SOLUBLE INTERCELLULAR ADHESION MOLECULE-1 AS MARKERS OF POSTOPERATIVE ORTHOPAEDIC JOINT PROSTHESIS INFECTIONS

L. DRAGO[1,2], C. VASSENA[1], E. DOZIO[3], M.M. CORSI[3], E. DE VECCHI[1], R. MATTINA[4] and C. ROMANÒ[5]

[1]Laboratory of Clinical Chemistry and Microbiology, IRCCS Galeazzi Institute, Milan; [2]Department of Clinical Science L. Sacco, University of Milan; [3]Department of Human Morphology and Biomedical Sciences "Città Studi", Laboratory of Clinical Pathology, University of Milan; [4]Department of Public Health, Microbiology and Virology, University of Milan; [5]Centre of Reconstructive Surgery and Osteoarticular Infections, IRCCS Galeazzi Institute, Milan, Italy

Received December 21, 2010 – Accepted April 14, 2011

There is a universally recognized need to identify new, reliable markers of inflammation that can aid in the rapid diagnosis of orthopaedic joint prosthesis infections (OJP-Is). Since prompt diagnosis is key to timely intervention in the course of infection, different molecules have been studied. In this study, we examined three groups of patients: those with prosthesis infection, those without infection, and a third group with previous infection in whom the infection had been cleared. Four presumed markers of infection were tested: procalcitonin (PCT); C-reactive protein (CRP); interleukin-6 (IL-6); and soluble intercellular adhesion molecule-1 (sICAM-1). The results showed that PCT cannot be considered as a good marker of periprosthetic infection as no statistically significant difference in serum PCT levels emerged between patients with infection and controls or patients without infection. In contrast, both sICAM-1 and CRP may be considered as good markers of infection, as measurement of their levels allowed us to distinguish between patients with and without infection, and between patients with infection and those with previous infection, since marker levels quickly returned to baseline values after clearance of the infection. IL-6 was found to be a good marker for inflammation, as it distinguished between patients with infection and the other groups. In the patients with previous infection, the IL-6 values remained high versus the controls but lower and with a statistically significant difference versus the patients with infection. Further studies are needed to determine the cut-off value of IL-6 between patients with infection and those with previous infection.

0394-6320 (2011)

USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE IN CHILDREN WITH RECURRENT ACUTE OTITIS MEDIA IN ITALY

P. MARCHISIO[1], S. BIANCHINI[1], C. GALEONE[2,3], E. BAGGI[1], E. ROSSI[1], G. ALBERTARIO[1], S. TORRETTA[4], L. PIGNATARO[4], S. ESPOSITO[1] and N. PRINCIPI[1]

[1]Department of Maternal and Paediatric Sciences,Università degli Studi di Milano and Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan; [2]Department of Epidemiology, Istituto di Ricerche Farmacologiche Mario Negri, Milan; [3]Department of Occupational Health "Clinica del Lavoro Luigi Devoto", Section of Medical Statistics "Giulio A. Maccacaro", Università degli Studi di Milano, Milan; [4]Department of Specialistic Surgical Sciences, Università degli Studi di Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Received January 9, 2011 – Accepted March 21, 2011

Controlling environmental factors, chemoprophylaxis, immunoprophylaxis and surgery are considered possible means of preventing recurrent acute otitis media (RAOM), but there are no available data concerning the paediatric use of complementary and alternative medicine (CAM). We evaluated the uses of CAM (homeopathy and/or herbal medicine) as means of preventing AOM in children with a history of RAOM. Eight hundred and forty Italian children with RAOM (≥3 episodes in six months) aged 1-7 years were surveyed in 2009 using a face-to-face questionnaire, filled by parents or caregivers, that explored the prevalence, determinants, reasons, cost, and perceived safety and efficacy of CAM. About one-half (46%) of the children used CAM, significantly more than the number who used immunoprophylaxis (influenza vaccine 15%; p<0.05), PCV-7 34%; p< 0.05) or chemoprophylaxis (2%; p<0.001). Use of CAM in the family was the only important factor positively associated with the use of CAM in children (adjusted OR 7.94; 95% CI: 5.26-11.99). The main reasons for using CAM were a fear of the adverse effects of conventional medicine (40%) and to increase host defences (20%). CAM was widely seen as safe (95%) and highly effective (68%). CAM prescribers were paediatricians in 50.7% of cases; self-initiation was reported by 23% of respondents. CAM expenditure was between €25 and €50/ month in 27.6% of cases and ≥ €50/month in 16%. Children with RAOM should be considered among the categories of subjects likely to be using CAM. Together with the fact that paediatricians are the main prescribers, this is worrying because of the current lack of evidence regarding the efficacy, safety and cost-effectiveness of CAM in the prevention of RAOM.

0394-6320 (2011)

INFLAMMATORY CELLS, CYTOKINES AND MATRIX METALLOPROTEINASES IN AMICROBIAL PUSTULOSIS OF THE FOLDS AND OTHER NEUTROPHILIC DERMATOSES

A.V. MARZANO[1], M. CUGNO[2], V. TREVISAN[1], R. LAZZARI[1], D. FANONI[1], E. BERTI[1] and C. CROSTI[1]

[1]Unità Operativa di Dermatologia, Fondazione IRCCS Ca' Granda – Ospedale Maggiore Policlinico, Dipartimento di Anestesiologia, Terapia Intensiva e Scienze Dermatologiche, Università degli Studi di Milano; [2]Dipartimento di Medicina Interna, Università degli Studi di Milano, Fondazione IRCCS Ca' Granda – Ospedale Maggiore Policlinico, Milano, Italy

Received January 5, 2011 – Accepted April 14, 2011

Amicrobial pustulosis of the folds (APF) is a rare cutaneous disease characterized by relapsing sterile pustules frequently associated with autoimmune disorders. Although APF pathophysiology is still undefined, scattered reports suggest involvement of neutrophils. The aim of the present study is to evaluate the role of the skin inflammatory infiltrate, selected multifunctional cytokines and effectors of tissue damage in APF and other neutrophilic dermatoses. We studied, by immunohistochemical methods, inflammatory cell markers (CD3, CD163, myeloperoxidase), cytokines (TNF-α, IL-8, IL-17), metalloproteinases (MMP-2, MMP-9) and vascular-endothelial-growth-factor (VEGF) in lesional skin from six patients with APF, 11 with pyoderma gangrenosum (PG), 7 with Sweet's syndrome, and in 20 normal skin samples. Immunoreactivities of CD3, CD163, myeloperoxidase, TNF-α, IL-8, IL-17, MMP-2, MMP-9 and VEGF were significantly higher in APF, PG and Sweet's syndrome than in controls (p=0.0001). IL-8 was more expressed in PG than in APF (P=0.002) and Sweet's syndrome (p=0.001). In APF, MMP-9 reactivity was higher than in Sweet's syndrome (p=0.035), but less intense than in PG (p=0.020). Our study supports the role of proinflammatory cytokines/chemokines and MMPs as important effectors for the tissue damage in APF similarly to classic neutrophilic dermatoses.

0394-6320 (2011)

PROGNOSTIC IMPLICATION OF HIGH RISK HUMAN PAPILLOMAVIRUS E6 AND E7 mRNA IN PATIENTS WITH INTRAEPITHELIAL LESIONS OF THE CERVIX IN RELATIONSHIP TO AGE

A. FREGA[1], L. LORENZON[2], M.R. GIOVAGNOLI[3], L. DE SANCTIS[1], V. FABIANO[3], A. LUKIC[1], M. MOSCARINI[1], M.R. TORRISI[3] and D. FRENCH[3]

[1]Department of Woman's Health and Territorial Medicine, Sant'Andrea Hospital, Faculty of Medicine and Psychology, Sapienza University of Rome; [2]Surgical and Medical Department of Clinical Sciences, Biomedical Technologies and Translational Medicine, Faculty of Medicine and Psychology, Sapienza University of Rome; [3]Department of Clinical and Molecular Medicine, Faculty of Medicine and Psychology, Sapienza University of Rome

Received November 17, 2010 – Accepted April 18, 2011

Since the introduction of the cytological screening programs, a significant reduction in the incidence of cervical cancer has been achieved. Almost all of these cancers are related to high-risk (HR) Human Papillomavirus (HPV) cervical infections. However, the natural history of HPV infection seems to be different in younger patients, resulting in a higher rate of regression. There is, therefore, the need to identify HPV-related biomarkers in order to enhance the effectiveness of screening of high-risk cytological lesions, in particular in women over 35 years of age. This study aims to evaluate the prognostic value of the HR HPV E6 and E7 mRNA expression in women with intraepithelial lesions of the cervix, older or younger than 35 years of age. One hundred and eighty-four HR HPV DNA positive patients with a low squamous intraepithelial lesion (LSIL) were tested for mRNA expressions, included in an observational study, and evaluated at follow-up with standard cytology up to 24 months from the mRNA test. The frequency of HSIL/LSIL cytology in the older cohort of mRNA positive patients was significantly higher compared to mRNA-negative patients, both at 1 and 2 years of follow-up (*Chi*-square: p 0.007 and p 0.009), but this difference was not found in the younger cohort. According to our results, the E6/E7 mRNA test could be a biomarker for viral activity, useful in identifying patients at higher risk of abnormal cytology, and in implementing the management of HR HPV DNA-positive women over 35 years of age.

0394-6320 (2011)

EXHALED NITRIC OXIDE LEVELS IN CHILDREN WITH CHRONIC ADENOTONSILLAR DISEASE

S. TORRETTA[1], P. MARCHISIO[2], S. ESPOSITO[2], W. GARAVELLO[3], M. CAPPADONA[1], I.A. CLEMENTE[1] and L. PIGNATARO[1]

[1]Otorhinolaryngological Clinic, Department of Specialist Surgical Sciences, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Milan; [2]Pediatric Clinic, Department of Maternal and Pediatric Sciences, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milano, Milan; [3]Otorhinolaryngological Clinic, DNTB, University of Milan-Bicocca, Monza, Italy

Received December 28, 2010 – Accepted April 27, 2011

Exhaled nitric oxide (eNO) is a highly reactive biological mediator that has recently been associated with chronic tonsillar disease in adults, but there are no published data concerning eNO levels in their pediatric counterparts. The aim of this study is to measure mean eNO levels in children with chronic adenotonsillitis or adenotonsillar hypertrophy, and assess the effects of potential confounding factors. Children aged 3-17 years were divided into three groups (chronic adenotonsillitis, adenotonsillar hypertrophy and controls). Their eNO levels were measured in accordance with the international guidelines, and their other clinical and anamnestic characteristics were recorded. The mean eNO level in the children with chronic adenotonsillitis was slightly higher than that in the other groups, but there was no statistically significant between-group difference. Age (p=0.009), allergy (p=0.05) and body mass index (p=0.03), but not the mean grade of adenoidal or tonsil hypertrophy, were all statistically related to mean eNO levels. These preliminary results indicate the lack of an increase in mean eNO levels in children with chronic adenotonsillar disease, with no substantial difference between children with chronic adenotonsillitis and those with adenotonsillar hypertrophy.

0394-6320 (2011)

ANTI-LAMININ-1 ANTIBODIES IN SERA AND FOLLICULAR FLUID OF WOMEN WITH ENDOMETRIOSIS UNDERGOING *IN VITRO* FERTILIZATION

D. CACCAVO[1,3], N.M. PELLEGRINO[1], I. TOTARO[2], M.P. VACCA[2], L. SELVAGGI[2] and R. DEPALO[2]

[1]Department of Clinical Medicine, Immunology and Infectious Diseases, University of Bari "Aldo Moro", Bari; [2]Department of Gynaecology, Obstetrics and Neonatology, Unit of Pathophysiology of Human Reproduction and Gametes Cryopreservation, University of Bari "Aldo Moro", Bari, Italy

Received February 22, 2011 – Accepted April 28, 2011

There is increasing evidence that autoimmune phenomena, including auto-antibody production, may affect fertility in women with endometriosis. The aims of this study are to evaluate anti-laminin-1 antibody (aLN-1) presence in sera and in follicular fluids (FF) of women with endometriosis undergoing IVF and its impact on oocyte maturation and IVF outcome. aLN-1 were measured by a home-made enzyme linked immunosorbent assay in sera and FF obtained from 35 infertile women with endometriosis and in sera from 50 fertile controls and 27 infertile women without endometriosis (IWWE). aLN-1 serum levels were significantly higher in women with endometriosis in comparison with both fertile controls and IWWE ($P<0.001$ and $P<0.05$, respectively) and a positive correlation was found between serum- and FF- aLN-1 ($r = 0.47$, $P = 0.004$). According to the cut-off (mean+3 SD of fertile controls), 31% of women with endometriosis were aLN-1 positive. Metaphase II oocyte counts showed inverse correlation with FF-aLN-1 levels ($r = -0.549$, $P = 0.0006$). Ongoing pregnancy (i.e pregnancy progressing beyond the 12th week of gestation) occurred in 4/11 aLN-1 positive patients and in 7/24 aLN-1 negative with no significant difference ($P= 0.7$). In conclusion, our results highlight that aLN-1 are increased in women with endometriosis and their presence in FF may affect oocyte maturation leading to a reduced fertility. However, aLN-1 seem to have no effect on IVF outcome.

0394-6320 (2011)

GLOBAL ACETYLATION AND METHYLATION CHANGES PREDICT PAPILLARY UROTHELIAL NEOPLASIA OF LOW MALIGNANT POTENTIAL RECURRENCE: A QUANTITATIVE ANALYSIS

R. MAZZUCCHELLI[1], M. SCARPELLI[1], A. LOPEZ-BELTRAN[2], L. CHENG[3], H. BARTELS[4], P.H. BARTELS[4], D.S. ALBERTS[4] and R. MONTIRONI[1,4]

[1]Section of Pathological Anatomy, Polytechnic University of the Marche Region, School of Medicine, United Hospitals, Ancona, Italy; [2]Department of Pathology, Reina Sofia University Hospital and Faculty of Medicine, Cordoba, Spain; [3]Department of Pathology and Laboratory Medicine, Indiana University School of Medicine, Indianapolis, IN, USA; [4]College of Public Health, Arizona Cancer Center, University of Arizona, USA

Received January 11, 2011 – Accepted April 28, 2011

The first two authors contributed equally to this work

Papillary urothelial neoplasia of low malignant potential (PUNLMP) recurs in approximately 35% of patients. Conventional histopathological assessment does not distinguish non-recurrent from recurrent PUNLMP. The aim of this study is to explore the differences in global histone acetylation and global DNA methylation between non-recurrent and recurrent PUNLMP. Acetylated histone H3 lysine 9 (AcH3K9) and 5-methylcytosine (5MeC) were investigated by immunohistochemistry (IHC) in 20 PUNLMP cases (10 non-recurrent and 10 recurrent), in 5 cases of normal urothelium (NU) and in 5 cases of muscle invasive pT2 urothelial carcinoma (UC). The total optical density of the nuclear staining was measured photometrically in at least 40 nuclei separately for the basal, intermediate and luminal positions in each case. Concerning the total optical density values for both acetylation and methylation, a decrease in staining is observed from non-recurrent PUNLMP to recurrent PUNLMP, at all nuclear locations. For acetylation the mean value in non-recurrent PUNLMP, intermediate between NU and UC, is closer to the former than to latter. The mean value in recurrent PUNLMP is closer to UC than to NU. In NU, non-recurrent and recurrent PUNLMP, the acetylation to methylation ratio decreased from the nuclei in basal position to those in the surface, the average for the above groups being 1.491, 1.611 and 1.746, respectively. Setting the observed values for NU at each sampling location to unity, acetylation shows a steady decrease, the percentages of changes in this nuclear location compared to NU being -5% in non-recurrent PUNLMP, -15% in recurrent PUNLMP and –24% in UC. Concerning methylation, there is a slight increase in non-recurrent PUNLMP (+5%), a decrease in recurrent PUNLMP (-19%) followed by a sharp rise for the UC (+61%). In conclusion, there are differences in global histone acetylation and DNA methylation patterns between non-recurrent and recurrent PUNLMP. Further studies are needed to elucidate the complex interplay between chromatin structure, its modifications and recurrence of PUNLMP.

0394-6320 (2011)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 24, no. 2, 499-504 (2011)

LETTER TO THE EDITOR

IMMUNOGENICITY OF AN INTERFERON-β1a PRODUCT

M.A. KAUFFMAN[1], A. STERIN-PRYNC[2], M. PAPOUCHADO[2], E. GONZÁLEZ[3], A.J. VIDAL[2], S.E. GROSSBERG[4], S. CHUPPA[4], B. ODORIZ[5], C. VRECH[6], R.A. DIEZ[2] and H.H. FERRO[2]

[1]Servicio de Neurología, Sanatorio V Franchin, Buenos Aires; [2]Bio Sidus S.A., Buenos Aires; [3]Centro de Diagnóstico Molecular, Buenos Aires; [4]Department of Microbiology & Molecular Genetics, Medical College of Wisconsin, Milwaukee, Wisconsin, U.S.A; [5]Hospital Central, Departamento de Neurociencias, Universidad Nacional de Cuyo, Mendoza; [6]Servicio de Neurología, Sanatorio Allende, Córdoba, Argentina

Received December 2, 2010 – Accepted April 14, 2011

In order to determine whether Blastoferon®, a biosimilar interferon (IFN)-β1a formulation, shares epitopes with other known IFN-β products, a series of neutralization bioassays were performed with a set of well-characterized anti-IFN-β monoclonal antibodies and human sera (World Health Organization Reference Reagents). The bioassay was the interferon-induced inhibition of virus cytopathic effect on human cells in culture (EMC virus and A-549 cells). Computer-calculated results were reported as Tenfold Reduction Units (TRU)/ml. To further assess Blastoferon® immunogenicity, in vivo production of anti-IFN ß antibodies was determined in sera of patients included in the pharmacovigilance plan of Blastoferon® by the level of IFN-ß1a binding antibodies (by enzyme immunoassay -EIA) and neutralizing antibodies (in the Wish-VSV system). The highly characterized neutralizing monoclonal antibodies A1 and A5 that bind to specific regions of the IFN-β molecule reacted positively with the three β1a IFNs: Blastoferon®, Rebif®, and the IFN-β WHO Second International Standard 00/572. As expected, the non-neutralizing monoclonal antibodies B4 and B7 did not neutralize any of the IFN-β preparations. The commercially available monoclonal antibody B-02 reacted essentially equally with Rebif® and Blastoferon®. The WHO Reference Reagent human serum anti-IFN-β polyclonal antibody neutralized all the IFN-β products, whereas the WHO Reference Reagent human serum anti-IFN-α polyclonal antibody G037-501-572 appropriately failed to react with any of the IFN-β products. On the basis of in vitro reactivity with known, well-characterized monoclonal and polyclonal antibody preparations, Blastoferon® shares immunological determinants with other human interferon-β products, especially IFN-β1a. In vivo antibodies were detected by EIA in 72.9% of 37 chronically treated multiple sclerosis patients, whereas neutralizing antibodies were found in 8.1% of them. Blastoferon® appears to have immunological characteristics comparable to other IFN-β1a products.

0394-6320 (2011)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 24, no. 2, 505-508 (2011)

LETTER TO THE EDITOR

ADENOSINE A2A RECEPTOR POLYMORPHISMS IN KOREAN PATIENTS WITH SYSTEMIC SCLEROSIS

J.A. PARK[1], J.J. PAK[4], J. KIM[1], E.Y. LEE[1], Y.J. LEE[1], Y.W. SONG[1] and E.B. LEE[1,2,3]

[1]Department of Internal Medicine, [2]Department of Immunology, Seoul National University College of Medicine, Seoul, Korea; [3]Medical Research Center, Seoul National University; [4]Department of Psychology, Columbia University, New York, U.S.A.

Received January 4, 2011 – Accepted April 15, 2011

Adenosine A2A receptor (ADORA2A) regulates inflammation, promotes tissue repair and collagen production by human dermal fibroblasts. We investigated the genetic polymorphisms of ADORA2A in susceptibility to systemic sclerosis (SSc). We genotyped 142 Korean SSc patients and 150 controls for polymorphisms of -1751A/C (rs5996696) and 1976C/T (rs5751876), to cover the promoter and all exon sequences of ADORA2A in Koreans, using TaqMan fluorogenic 5' nuclease assay and single base primer extension assay. Neither -1751A/C nor 1976C/T polymorphism showed difference in the distribution of alleles or genotypes between patients and controls with allele frequency of 89.9% *v* 91.0% for -1751A (p=0.64) and 56.5% *v* 54.0% for 1976C (p=0.55). Our findings suggest that the role of ADORA2A in SSc may not be genetically related.

0394-6320 (2011)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 24, no. 2, 509-515 (2011)

LETTER TO THE EDITOR

EXAGGERATED IMIQUIMOD APPLICATION SITE REACTIONS IN THE CONTEXT OF SYSTEMIC TUMOR NECROSIS FACTOR-ALPHA INHIBITION: MORE THAN A COINCIDENTAL OCCURRENCE?

A. SAGGINI, R. SARACENO and S. CHIMENTI

Department of Dermatology, University of Rome Tor Vergata, Rome, Italy

Received December 12, 2010 – Accepted April 6, 2011

Topical imiquimod and tumor necrosis factor (TNF)-α inhibitors have gained wide acceptance as safe and effective treatments for non-melanoma skin cancer (NMSC) and moderate to severe psoriasis, respectively. While mild to moderate application site reactions (ASRs) are a well-known and common phenomenon associated with imiquimod, the potential of TNF-α blockers to elicit cutaneous inflammatory reactions has only recently been recognized. We present two cases of severe, atypical ASRs which occurred during NMSC treatment with imiquimod in the context of infliximab administration for psoriasis, and consider the grounds supporting a non-fortuitous association. To date, no relation has ever been suggested between TNF-α inhibitors and increased susceptibility to developing exaggerated ASRs with imiquimod. We believe that this subject deserves further analysis; meanwhile, increased attention should be drawn to the possibility of this adverse interaction, as simultaneous treatment with TNF-α blockers and imiquimod is becoming increasingly frequent in daily practice.

0394-6320 (2011)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 24, no. 2, 517-518 (2011)

LETTER TO THE EDITOR

FRIDAY ASTHMA CRISIS IN THE DAUGHTER OF TWO BAKERS

S. CAIMMI[1], A. MARSEGLIA[2], D. CAIMMI[2] and G.L. MARSEGLIA[2]

[1]Department of Pediatrics, Azienda Ospedaliera Ospedale Maggiore di Crema, Cremona;
[2]Department of Pediatrics, Foundation IRCCS Policlinico San Matteo, University of Pavia, Italy

Received September 6, 2010 – Accepted March 9, 2011

The prevalence of sesame food allergy continues to increase worldwide. The diagnostic tools to confirm such allergy include skin prick tests, specific IgEs and food challenge. We report the case of a 7-year-old girl who presented recurrent episodes of wheezing and dyspnoea. After performing skin tests and evaluating specific IgEs we hypothesised an allergy to sesame. Our patient actually benefitted from avoiding any contact with sesame and sesame seeds. We confirmed our diagnosis through an inhalation food challenge. Further, by reviewing her personal history, we suspect inhalation was the mechanism in which the girl became sensitised to sesame.

0394-6320 (2011)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 24, no. 2, 519-522 (2011)

LETTER TO THE EDITOR

DIAGNOSTIC FAILURE OF CIPROFLOXACIN-INDUCED SPONTANEOUS BILATERAL ACHILLES TENDON RUPTURE: CASE-REPORT AND MEDICAL-LEGAL CONSIDERATIONS

A. PANTALONE[1], M. ABATE[2], C. D'OVIDIO[3], A. CARNEVALE[3] and V. SALINI[1]

[1]Orthopaedics Division, "G. d'Annunzio" University of Chieti; [2]Department of Neuroscience and Imaging, Infrared Imaging Laboratory, Institute of Advanced Biomedical Technologies (ITAB), "G. d'Annunzio" University of Chieti-Pescara; [3]Department of Medicine and Aging Science, Section of Legal Medicine, "G. d'Annunzio" University of Chieti-Pescara, Italy

Received November 22, 2010 – Accepted February 23, 2011

Rare side-effects of fluoroquinolone therapy are tendinitis and tendon rupture. Many reports have demonstrated that the concomitant use of corticosteroids, in patients aged 60 years or older, increase the risk substantially. We present a case of spontaneous bilateral Achilles tendon rupture induced by ciprofloxacin and methylprednisolone. A 61-year-old woman was diagnosed with Bronchiolitis Obliterans with Organizing Pneumonia (BOOP) and was started on oral ciprofloxacin 500 mg twice daily for 3 weeks and on oral methylprednisolone 16 mg twice daily for 2 weeks. The diagnosis was made after doctors, rather than stop drug therapy and advise complete rest, had mistakenly prescribed for the woman to undergo physiotherapy and local NSAIDs, thus favoring the onset of tendon ruptures and resulting in surgical and legal implications. Inspired by this case, we also submit a brief review on professional liability in Orthopaedics.

0394-6320 (2011)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 24, no. 2, 523-527 (2011)

LETTER TO THE EDITOR

ULERYTHEMA OPHRYOGENES, A RARE AND OFTEN MISDIAGNOSED SYNDROME: ANALYSIS OF AN IDIOPATHIC CASE

C. DIANZANI[1], A. PIZZUTI[2], F. GASPARDINI[1], L. BERNARDINI[2], B. RIZZO[2,3] and A.M. DEGENER[2,3]

[1]Department of Dermatology, Campus Bio-Medico University of Rome; [2]Department of Molecular Medicine, [3]Section of Virology, "Sapienza" University, Rome, Italy

Received October 26, 2010 – Accepted March 25, 2011

Keratosis pilaris (KP) is a follicular hyperkeratosis disorder which is frequently detected in the adult population (44%), mostly in female adolescents (80%). It is a genetic autodominant dermatosis with variable penetrance, but no specific gene association has been determined, even though association to the presence of chromosome 18p deletion has been reported in some cases. We report the case of a 51-year-old Caucasian woman affected by keratosis pilaris gradually progressing with age and with a story of multiple abortions. Standard karyotype and CGH array analyses did not reveale any genetic abnormality. Virological analyses detected the presence of HPV 36 DNA inside the dorsum biopsy, leading to hypothesize its involvement in the evolution of the lesion. Clinical history and patient examination led the diagnosis of an idiopathic case of Ulerythema ophryogenes. The analysis of more cases could be useful to verify the involvement of cutaneous HPV in the progression of the clinical manifestation of the KP variants.

0394-6320 (2011)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 24, no. 2, 529-534 (2011)

LETTER TO THE EDITOR

PLATELET AMYLOID PRECURSOR PROTEIN ISOFORM EXPRESSION IN ALZHEIMER'S DISEASE: EVIDENCE FOR PERIPHERAL MARKER

A. VIGNINI[1], D. SARTINI[1], S. MORGANTI[1], L. NANETTI[1], S. LUZZI[2], L. PROVINCIALI[2], L. MAZZANTI[1] and M. EMANUELLI[1]

[1]Department of Biochemistry, Biology and Genetics, School of Medicine, Polytechnic University of Marche, Ancona; [2]Department of Neuroscience, Polytechnic University of Marche, Ancona, Italy

Received October 26, 2010 – Accepted April 15, 2011

The first two authors contributed equally to this work

Alzheimer's disease (AD) is a chronic neurodegenerative disorder characterized by a progressive cognitive and memory decline. Among peripheral markers of AD, great interest has been focused on the amyloid precursor protein (APP). In this regard, platelets represent an important peripheral source of APP since it has been demonstrated that the three major isoforms, that are constituted of 770, 751 and 695 aa residues, are inserted in the membrane of resting platelets. APP 751 and APP 770 contain a Kunitz-type serine protease inhibitor domain (APP KPI) and APP 695 lacks this domain. To address this issue, we first examined the platelet APP isoform mRNAs prospectively as biomarker for the diagnosis of AD by means of real-time quantitative PCR, and then evaluated the correlation between APP mRNA expression levels and cognitive impairment of enrolled subjects. Differential gene expression measurements in the AD patient group (n=18) revealed a significant up-regulation of APP TOT (1.52-fold), APP KPI (1.32-fold), APP 770 (1.33-fold) and APP 751 (1.26-fold) compared to controls (n=22). Moreover, a statistically significant positive correlation was found between APP mRNA levels (TOT, KPI, 770 and 751) and cognitive impairment. Since AD definitive diagnosis still relies on pathological evaluation at autopsy, the present results are consistent with the hypothesis that platelet APP could be considered a potential reliable peripheral marker for studying AD and could contribute to define a signature for the presence of AD pathology.

0394-6320 (2011)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 24, no. 2, 535-537 (2011)

LETTER TO THE EDITOR

LACTOSE INTOLERANCE IN SYSTEMIC NICKEL ALLERGY SYNDROME

I.A. CAZZATO[1,2], E. VADRUCCI[2], G. CAMMAROTA[1], M. MINELLI[2] and A. GASBARRINI[1]

[1]Internal Medicine and Gastroenterology Unit, Internal Medicine Department, Gemelli Hospital, Catholic University of Sacred Heart, Rome; [2]IMID Unit, Internal Medicine Department, San Pio Hospital, Campi Salentina, Lecce, Italy

Received March 1, 2011 – Accepted April 15, 2011

Some patients affected by nickel-contact allergy present digestive symptoms in addition to systemic cutaneous manifestations, falling under the condition known as Systemic Nickel Allergy Syndrome (SNAS). A nickel-related pro-inflammatory status has been documented at intestinal mucosal level. The aim of the present study is to evaluate the prevalence of lactose intolerance in patients affected by SNAS compared to a healthy population. Consecutive patients affected by SNAS referring to our departments were enrolled. The control population consisted of healthy subjects without gastrointestinal symptoms. All subjects enrolled underwent lactose breath test under standard conditions. One hundred and seventy-eight SNAS patients and 60 healthy controls were enrolled. Positivity of lactose breath test occurred in 74.7% of the SNAS group compared to 6.6% of the control group. Lactose intolerance is highly prevalent in our series of patients affected by SNAS. Based on our preliminary results, we can hypothesize that in SNAS patients, the Nickel-induced pro-inflammatory status could temporarily impair the brush border enzymatic functions, resulting in hypolactasia. Further trials evaluating the effect of a nickel-low diet regimen on lactase activity, histological features and immunological pattern are needed.

0394-6320 (2011)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 24, no. 2, 539-544 (2011)

LETTER TO THE EDITOR

CERVICAL FOLLICULAR DENDRITIC CELL SARCOMA: A CASE REPORT AND REVIEW OF THE LITERATURE

M. PIZZI[1], K. LUDWIG[1], G. PALAZZOLO[2], G. BUSATTO[3], C. RETTORE[4] and G. ALTAVILLA[1]

[1]Department of Diagnostic Medical Sciences and Special Therapies University of Padova; [2]Division of Medical Oncology, U.L.S.S. 15 "Alta Padovana", Cittadella; [3]Department of Anatomic Pathology, U.L.S.S. 15 "Alta Padovana", Cittadella; [4]Division of Radiology, U.L.S.S. 15 "Alta Padovana", Cittadella, Padova, Italy

Received November 23, 2010 – Accepted April 28, 2011

Follicular dendritic cell (FDC) sarcoma is a rare tumour with a low-to-intermediate grade of malignancy. It frequently occurs in cervical, mediastinal and axillary lymph nodes. In approximately 30% of cases an extranodal localization has been reported (tonsils, oral cavity, mediastinum, liver, and spleen). Very little is known about possible treatment options and overall prognosis. This case reports a 66 year-old patient, who underwent surgical removal of a persistently enlarged right cervical lymph node. The histopathological examination revealed a spindle cell tumour with lymphocyte and plasma cell infiltrates. Neoplastic cells stained positive for CD21, CD23 and CD35, thus confirming the diagnosis of FDC sarcoma. The neoplasm recurred two years later and partial regression was achieved by IGEV rescue therapy. We briefly discuss clinical history, histopathological differential diagnosis and treatment options of FDC sarcoma.

0394-6320 (2011)

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 24, no. 2, 545-547 (2011)

LETTER TO THE EDITOR

ERYTHEMA MULTIFORME-LIKE IRRITANT CONTACT DERMATITIS AFTER APPLICATION OF AN ANTISCABIES TREATMENT

A. BASSI[1], A.M. D'ERME[1] and M. GOLA[2]

[1]Department of Dermatology II, University of Florence, Florence; [2]Allergological and Occupational Dermatology Unit, Florence, Italy

Received January 19, 2011 – Accepted April 26, 2011

We describe the case of an irritant contact dermatitis due to an antiscabies treatment in a man who presented to our clinic with an important cutaneous reaction with many hemorrhagic, "target" erythema multiforme-like lesions, as the result of an acute toxic insult of the skin by permethrin 5%. This is a possible, but very uncommon symptom of non-eczematous contact dermatitis and an unusual drug causing the acute hypersensitivity reaction typical of erythema multiforme.

0394-6320 (2011)